Impact of the 20-week scan

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Chapter 1

Introduction and aims of the thesis

INTRODUCTION

Approximately 2-3% of all pregnancies are complicated by congenital anomalies affecting the fetus (1-4). While in many cases fetal and neonatal deaths related to lethal congenital anomalies or extreme preterm birth are not preventable (5), in some cases prenatal diagnosis can improve outcome by optimizing the timing and mode of delivery and by preventing emergency transportation of the neonate after birth (6). Prenatal diagnosis also allows parents to consider the option of termination of pregnancy (2). Back in 1958 Ian Donald, an obstetrician, and Tom Brown, an engineer, first reported on prenatal ultrasound (1,6). In the following decades, improvements in technology, scanning techniques and diagnostics tests greatly increased the scope of ultrasound investigation from biometry, placental localization and diagnosis of multiple births to prenatal detection of congenital anomalies (1).With the introduction of routine ultrasound scanning during pregnancy, many congenital anomalies can now be detected prenatally (1,2,4,6-11).

The introduction of prenatal ultrasound screening in the Netherlands

In contrast to its fellow European countries, the Netherlands was late in offering routine prenatal ultrasound screening to all pregnant women. In 2004 a survey of prenatal screening policies in eighteen European countries reported that the Netherlands was one of four countries that did not offer routine prenatal ultrasound scans (7). When the introduction of routine ultrasound was first considered in 2001, the Dutch Health Council concluded that ultrasound was inferior to the triple test to screen for Down's syndrome and neural tube defects. In 2003, the ministry of Health summarized this view in a letter stating that the disadvantages of ultrasound screening (additional medical investigations and the possibility of a miscarriage due to diagnostic testing) did not outweigh the advantages (12). In 2004 the Dutch Health Council re-examined the scientific evidence and they issued an amended report (13). In this second report the council recommended first trimester screening for Down syndrome based on maternal blood analysis and fetal nuchal translucency measurement (combined test) and second trimester ultrasound screening for neural tube defects. The revised report describes that the combined studies available in 2004 provide sufficient evidence to conclude that ultrasound performs better than the triple test in screening for neural tube defects. Whether or not other anomalies besides neural tube defects could be diagnosed by routine ultrasound screening at about 20 weeks' gestation, could not be answered at that time (14). In the following years discussion about the organization of prenatal screening took place, resulting in a proposal for a national screening program in 2006 (15).

Legal background, counseling and financial issues

There are two legal acts that play a role in the Dutch prenatal screening program. The first act, the Dutch Population Screening Act ("WBO"), prescribes that screening for diseases without the possibility of treatment or prevention can only be performed after a special license is granted by the Ministry (16). Specifically for prenatal screening it has been added that termination of pregnancy should not be regarded as a form of prevention (14). In 2004, the government allowed information on risk assessment tests for Down's syndrome and neural tube defects but the screening was provisionally only free of charge for women with an increased a-priori risk (17). As per January 1, 2007 the eight regional screening centers linked to the prenatal diagnosis departments of the eight universities were granted a licence to perform prenatal ultrasound screening. Each regional center is responsible to guarantee uniformity inperformance of counselors and sonographers in their region. Moreover, to ensure optimal quality the Dutch Health Council proposed that the program is coordinated and monitored by the National Centre for Public Health and the Environment (13).

The second act, the Dutch Medical Treatment Act (WGBO), describes the rights and obligations of patients, including the right to receive or decline information (18). A pregnant woman cannot be exposed to unwanted and unsolicited screening tests and she has the right 'not to know'. Information about medical investigations must be provided in a manner that it is reasonably certain that parents understand the test to its content. Parents need to have sufficient time to make a carefully considered decision to authorize medical examinations. To comply with these requirements, healthcare providers first ask parents whether they want information on prenatal screening. Thereafter, written and oral information on the test characteristics is provided. National leaflets on first and second trimester screening became available in 2008.

To ensure free access for all women, the 20-week scan has been incorporated in the Basic Health Insurance package. This is not the case for the first trimester combined test; this test was only free for women aged 36 or older (note: since January 2015 all women, with the exception of those at high-risk based on medical history and/or previous pregnancies, have to pay for the combined test, irrespective of age (19)).

Development of the goals of the screening program

The combined test in the first trimester was initially exclusively aimed at screening for Down's syndrome. In April 2011, trisomy 13 (Patau syndrome) and trisomy 18 (Edwards syndrome) were officially added (20). The primary aim of the 20-week scan was the detection of neural tube defects (21), although it was recognized that other anomalies may be visualized. Examples of major anomalies that are amenable to ultrasound diagnosis are congenital heart defects, congenital diaphragmatic hernia, abdominal wall defects, kidney anomalies and skeletal anomalies. In addition, the sonographer may note unexpected minor anomalies

during the 20-week scan ('softmarkers'). Typical for these markers is that they are not pathological in itself, but they are more often observed in abnormal fetuses and therefore their finding increases the likelihood of an abnormal outcome warranting additional investigations (3,22,23). However, the positive predictive value of softmarkers is low (23). The Dutch Society for Obstetricians and Gynaecologists therefore issued a management protocol. In the case of isolated ventriculomegaly, hyperechogenic bowel, pyelectasis of at least 10 mm, short femur and a single umbilical artery women should be referred to a fetal medicine unit for an advanced ultrasound scan. In case of mild pyelectasis (5 to 10 mm), a repeat scan at 32 weeks of gestation is recommended. No action is required when a choroid plexus cyst or intracardiac focus are seen, these are considered normal anatomic variations.

High risk group and prenatal diagnosis

Women that are at increased risk for a child with a congenital anomaly because of their medical history or a previous pregnancy are offered an advanced 20- week anomaly scan at a fetal medicine unit. An advanced diagnostic scan at a fetal medicine unit is offered if a congenital anomaly is suspected during the 20-weeks scan and when indicated additional investigations and genetic testing are offered. If needed, a pediatric specialist such as a cardiologist, surgeon or neurologist will be present at the detailed scan and counsel parents jointly with the fetal medicine specialist. Parents are immediately counseled on the findings and, when this is considered appropriate, genetic testing is offered. In 2011 array-CGH analysis was introduced in the Netherlands. Prior to that only conventional karyotyping was offered (24).

Uniform training, protocol and counseling

After the license was granted all the (inexperienced) sonographers and counselors were trained within a short period of time to meet the requirements of the screening program. Counselors are required to attend one of the special courses developed by the regional centers and complete the National Prenatal Screening Course for counselors ("DIN"). The protocol for the combined test and the 20-week scan developed by the Dutch Society for Obstetricians and Gynaecologists in 2005 were taken as the gold standard. This protocol for the 20-week scan included not only assessment of markers of neural tube defects but it required examination of the entire fetal anatomy with a few items being marked "optional". In 2012, the optional items (assessment of the upper lip, the position of the aorta and pulmonary artery and three-vessel view) became part of the standard protocol (25).

Monitoring

Prenatal ultrasound screening in the Netherlands is monitored by the National Centre for Public Health and the Environment. In collaboration with the eight Regional Centers for

Prenatal Ultrasound Screening, national protocols were developed and an annual evaluation was implemented both on a regional and a national level. Health care providers can only obtain a contract with the Regional Centre and participate in the screening program if they fulfill the educational criteria and if they submit data and images for audit (26).

Development of a national database

From the start of the screening program, accredited counselors and sonographers were required to collect data on their screening activities (counseling, combined test and 20-week scan), in order to document and potentially improve the primary process of prenatal screening (27). For the purpose of data collection and monitoring a national database named, Peridos (28) was developed which became operational in 2010. Due to compatibility issues it was not until 2012 that data in Peridos could be used for assessment (29,30). In 2014, 96.6% of the 20-week scans that were performed were uploaded in Peridos (31). Annual reports are published with the primary aim 'to study and describe national and regional numbers with regards to the screening program based on a set of indicators'. Examples of reported indicators are: number of scans per region, participation percentage for combined test and mid-trimester scan after counseling, number of repeated exams and number of scans per sonographer.

Aims and methods of this thesis

In this thesis the results of a study examining the efficacy of the 20-week scan in identifying four congenital anomalies is described. The first aim is to examine timing of diagnosis and outcome of cases with neural tube defects (open spina bifida and anencephaly), abdominal wall defects (gastroschisis and exomphalos), cleft lip (with or without cleft palate) and congenital heart defects since a national screening program was introduced. The second aim is to assess the prevalence and significance of three softmarkers (ventriculomegaly, echogenic bowel and single umbilical artery) when found as an isolated finding during the 20-week scan.

In the Northeast data was collected from the regional center (SPSNO) associated to the University Medical Center Groningen (UMCG) and in the Northwest from the regional center (SPSAO) associated with the Academic Medical Center in Amsterdam (AMC), together representing approximately 20% of the annual births in the Netherlands. Pre-and postnatal cases of the selected congenital anomalies were identified from first and second trimester screening datasets (including basic outcome details on type of birth and the presence of congenital anomalies, if any) and advanced diagnostic scans. Cytogenetic findings were added to the case lists. Case lists from pediatric surgeons and in the Northeast data from EUROCAT (European Registry of Congenital Anomalies and Twins) Northern Netherlands (32), a population-based birth defects registry was used to complement the dataset. Data on

children that were registered with one of the specialized cleft-teams in the area was provided by the Dutch Association for Cleft Palate and Craniofacial Anomalies (33). Pregnancy outcome was provided by the Netherlands Perinatal Registry (34). Uptake of the 20-week scan was calculated on prospectively collected data on pregnancies with an estimated date of delivery in the years 2012 – 2014 from the three Northern provinces (Groningen, Friesland and Drenthe). In this dataset prevalence and outcome of the three selected isolated soft markers was examined.

Outline thesis

The first area of investigation was the assessment of the efficacy of the 20-week anomaly scan in detecting neural tube defects. Chapter 2 describes detection and pregnancy outcome for open spina bifida during the years 2003 and 2011. Results for a study on the detection of anencephaly during the years 2008 – 2013 are presented chapter 3. The prenatal detection and pregnancy outcome of abdominal wall defects during 2009 – 2013 is summarized in chapter 4 and chapter 5 reports on the accuracy of prenatal assessment and registration of cleft lip in the Netherlands during the years 2008 – 2012. Results of a collaboration with the Academic Center of Utrecht on the prenatal diagnostic accuracy of congenital heart defects and difference between pre-and postnatal diagnosed cases in the period 2008- 2013 is described in chapter 6. In a systematic review the relationship of isolated single umbilical artery to fetal growth, aneuploidy and perinatal mortality was examined, which is described in chapter 7. In chapter 8 uptake of the 20-week scan and the prenatal detection rate of the selected group of congenital anomalies and isolated soft markers for a three year period (2012 – 2014) is described. A summary, general discussion as well as future recommendations can be found in chapter 9.

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